

CLAIMS

1. Use of a pluripotent cell that expresses the *Hox11* gene in the preparation of a medicament for increasing or maintaining the number of functional cells of a predetermined type in an organ or tissue of a mammal, wherein said organ or tissue is injured, damaged, or deficient in said functional cells.
2. The use of claim 1, wherein said pluripotent cell is derived from a pluripotent or totipotent cell transfected with a *Hox11* gene.
3. The use of claim 1, wherein said pluripotent cell is enriched in cells that do not express CD45.
4. The use of claim 3, wherein said pluripotent cell is obtained from the peripheral blood or tissue of a mammal by a method comprising:
 - a) providing from the mammal peripheral blood or tissue containing pluripotent cells;
 - b) separating pluripotent cells from said peripheral blood or tissue;
 - c) separating said pluripotent cells into a first cell population which predominantly expresses CD45 antigen on the surface of said cells and a second cell population which predominantly does not express CD45 antigen on the surface of said cells; and
 - d) selecting said second cell population.
5. The use of any of the claims 1-4, wherein said pluripotent cell is derived from the spleen.

6. Use of a CD45(-) pluripotent cell in the preparation of a medicament for increasing or maintaining the number of functional cells of a predetermined type in an organ or tissue of a mammal, wherein said organ or tissue is injured, damaged, or deficient in said functional cells, with the proviso that said pluripotent cell is not a bone marrow cell or a muscle cell.

7. The use of claim 6, wherein said pluripotent cell is selected from the group consisting of: peripheral lymphocyte, cord blood cell, and splenocyte.

8. The use of claim 7, wherein said pluripotent cell is a splenocyte.

9. The use of claim 6-8, wherein said pluripotent cell is obtained by a method comprising:

- a) providing from the mammal spleen tissue containing pluripotent cells;
- b) separating pluripotent cells from said spleen tissue;
- c) separating said pluripotent cells into a first cell population which predominantly expresses CD45 antigen on the surface of said cells and a second cell population which predominantly does not express CD45 antigen on the surface of said cells; and
- d) selecting said second cell population.

10. The use of any of the claims 1-9, wherein said pluripotent cell is semi-allogeneic.

11. The use of any of the claims 1-9, wherein said pluripotent cell is isogeneic.

12. The use of any of the claims 1-9, wherein said organ or tissue is stimulated.
13. The use of any of the claims 1-12, wherein said pluripotent cell presents MHC class I and peptide, wherein said MHC class I has at least one allele that matches an MHC class I allele expressed by said mammal.
14. The use of any of the claims 1-12, wherein said pluripotent cell contains one or more cell surface markers selected from the group consisting of: retinoic acid receptor, estrogen receptor, EGF receptor, CD49b, VLA2, CD41, LFA-1, ITB2, CD29, NTC3 receptor, plasminogen receptor, transferrin receptor, TGF receptor, PDGF receptor, thyroid growth hormone receptor, and integrin beta 5.
15. The use of any of the claims 1-14, said medicament further comprising a second agent that selectively inhibits, removes, or kills a cell population that interferes or prevents the trafficking of, differentiation of, or growth of said pluripotent cell.
16. The use of claim 15, wherein said cell population that interferes or prevents the trafficking of, differentiation of, or growth of said pluripotent cell comprises T-lymphocytes.
17. The use of claim 15, wherein said second agent is TNF-alpha.
18. The use of claim 15, wherein said second agent is a TNF-alpha agonist or a TNF-alpha inducing substance.

19. The use of claim 18, wherein said TNF-alpha agonist or TNF-alpha inducing substance is Complete Freund's Adjuvant (CFA), ISS-ODN, microbial cell wall components with LPS-like activity, cholera particles, *E. coli* heat labile enterotoxin, *E. coli* heat labile enterotoxin complexed with lecithin vesicles, ISCOMS-immune stimulating complexes, polyethylene glycol, poly(N-2-(hydroxypropyl)methacrylamide), synthetic oligonucleotides containing CpG or CpA motifs, monophosphoryl lipid A, *Bacillus Clamette-Guerin*, γ -interferon, Tissue Plasminogen Activator, LPS, Interleukin-1, Interleukin-2, UV light, a lymphotoxin, cachectin, a TNFR-1 agonist, a TNFR-2 agonist, an intracellular mediator of the TNF-alpha signaling pathway, a NF κ B inducing substance, IRF-1, STAT1, a lymphokine, or the combination of TNF-alpha and an anti-TNFR-1 antibody.

20. The use of claim 19, wherein said TNF-alpha agonist or TNF-alpha inducing substance is Complete Freund's Adjuvant, *Bacillus Clamette-Guerin*, or γ -interferon.

21. Use of an agent in the preparation of a medicament for increasing or maintaining the number of functional cells of a predetermined type in an organ or tissue of a mammal, wherein said organ or tissue is injured, damaged, or deficient in said functional cells and said agent induces *Hox11*-expressing pluripotent cells.

22. The use of claim 17, wherein said *Hox11*-expressing pluripotent cells do not express CD45.

23. The use of claims 21 or 22, wherein said agent is a gene therapy vector comprising a *Hox 11* gene operably linked to a promoter, wherein said vector expresses *Hox 11* in said pluripotent cells.

24. The use of claims 21 or 22, wherein said *Hox11*-expressing pluripotent cells are not bone marrow cells.

25. Use of an agent in the preparation of a medicament for increasing or maintaining the number of functional cells of a predetermined type in an organ or tissue of a mammal, wherein said organ or tissue is injured, damaged, or deficient in said functional cells and said agent induces pluripotent cells that do not express CD45.

26. The use of any of the claims 21, 22, 24, and 25, wherein said agent is, or induces in said mammal, a cytokine, chemokine, or growth factor.

27. The use of claim 26, wherein said cytokine, chemokine, or growth factor is selected from the group consisting of: epidermal growth factor (EGF), platelet-derived growth factor (PDGF), fibroblast growth factors (FGFs), transforming growth factor-beta (TGF- β), transforming growth factor-alpha (TGF- α), vascular endothelial growth factor (VEGF), erythropoietin (Epo), insulin-like growth factor-I (IGF-I), insulin-like growth factor-II (IGF-II), interleukins, tumor necrosis factor-alpha (TNF- α), tumor necrosis factor-beta (TNF- β), interferon-gamma (INF- γ), stromal cell-derived factor-1 (SDF-1), and a colony stimulating factors (CSF).

28. The use of any of the claims 1-27, wherein said organ or tissue is, or is part of, the pancreas, the spleen, the liver, the kidney, nerve tissue, or the bone.

29. The use of claim 28, wherein said organ or tissue is, or is part of, the pancreas.

30. Use of an agent for in the preparation of a medicament for increasing or maintaining the number of functional cells of a predetermined type in an organ or tissue of a mammal, wherein said organ or tissue is injured, damaged, or deficient in said functional cells and said agent selectively inhibits, removes, or kills cell populations that interfere with or prevent the trafficking of, differentiation of, or growth of pluripotent cells.

31. The use of claim 30, wherein said agent targets a cell population deficient in the expression of CD180.

32. The use of claim 31, wherein said agent is BCG, LPS, a triacetylated lipopeptide, phenol-soluble modulin, or OspA LP from *B. burgdorferi*, a triacetylated lipopeptide with TLR1 or TLR6, HSP60 with TL4, HSP60, a mannuronic acid polymer, a flavolipin, a tecihuronic acid, neumolysin, fimbriae, surfactant protein A, hyaluronan, heparin sulfate or a heparin sulfate fragment, a fibrinogen peptide, beta-defensin-2, flagellin, or imidazolquinoline,

33. The use of claim 30, wherein said pluripotent cells express *Hox 11*.

34. The use of claim 30, wherein said pluripotent cells do not express CD45.

35. The use of claim 30, wherein said pluripotent cells are isogenic.

36. The use of claim 30, wherein said pluripotent cells are semi-allogeneic.

37. The use of any of the claims 1-36, wherein said mammal has an autoimmune disease.

38. The use of claim 37, wherein said disease is diabetes.
39. The use of claim 37, wherein said disease is immunologically-mediated glomerulonephritis.
40. The use of claim 37, wherein said disease is chronic hepatitis, primary biliary cirrhosis, or primary sclerosing cholangitis.
41. The use of any of the claims 1-36, wherein said tissue or organ is the pancreas, the salivary gland, the pituitary gland, a kidney, the heart, an olfactory gland, an ear, a bone, the liver, the brain, the peripheral nervous system, the central nervous system, the spinal cord, a mammary gland, or a testes.
42. An isolated CD45(-) pluripotent cell population, wherein at least 75% of the cells of said population express *Hox11*.
43. The pluripotent cell population of claim 42, wherein at least 90% of the cells of said population express *Hox11*.
44. An isolated *Hox11*-expressing pluripotent cell population, wherein at least 75% of the cells do not express CD45.
45. The pluripotent cell population of claim 44, wherein at least 90% of the cells of said population do not express CD45.

46. The pluripotent cell population of any of the claims 42-45, wherein the cells in said cell population contain one or more cell markers selected from the group consisting of: contains one of more cell surface markers selected from the group consisting of: retinoic acid receptor, estrogen receptor, EGF receptor, CD49b, VLA2, CD41, LFA-1, ITB2, CD29, NTC3 receptor, plasminogen receptor, transferrin receptor, TGF receptor, PDGF receptor, thyroid growth hormone receptor, and integrin beta 5.

47. The pluripotent cell population of any of the claims 42-45, wherein said cell population is obtained from the peripheral blood or tissue of a mammal by a method comprising:

- a) providing from the mammal peripheral blood or tissue that contains pluripotent cells;
- b) separating pluripotent cells from said peripheral blood or tissue;
- c) separating said pluripotent cells into a first cell population which predominantly expresses CD45 antigen on the surface of said cells and a second cell population which predominantly does not express CD45 antigen on the surface of said cells; and
- d) selecting said second cell population.

48. The pluripotent cell population of claim 47, wherein said cell population is further purified by separating said CD45(-) pluripotent cells into a third cell population which predominantly expresses a cell surface marker selected from the group consisting of: retinoic acid receptor, estrogen receptor, EGF receptor, CD49b, VLA2, CD41, LFA-1, ITB2, CD29, NTC3 receptor, plasminogen receptor, transferrin receptor, TGF receptor, PDGF receptor, thyroid growth hormone receptor, and integrin beta 5, and a fourth cell population which predominantly does not express said cell surface marker.

49. The pluripotent cell population of any of the claims 42-48, wherein said pluripotent cell population is derived from the spleen.

50. A pluripotent cell transfected with a *Hox11* gene, wherein said cell is capable of differentiating into a cell selected from the group consisting of: a pancreatic cell, a spleen cell, a liver cell, a kidney cell, a nerve cell, and a bone cell.

51. The cell of claim 50, wherein said cell is capable of differentiating into a pancreatic cell.

52. The cell of claim 50, wherein said cell is transfected with a human *Hox11* gene.

53. The cell of claim 50, wherein said pluripotent cell is derived from the spleen.

54. The cell of claim 50, wherein said pluripotent cell is derived from cord blood.

55. The cell of any of the claims 50-54, wherein said pluripotent cell does not express CD45.